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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,392	09/08/2000	Charles W. Ford	6137.P US	4850

7590 05/08/2002

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/08/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/600,392	Applicant(s) FORD ET AL.	
	Examiner Gerald G Leffers Jr.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-77* is/are pending in the application.

4a) Of the above claim(s) *21-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-20 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-20 and 77) in Paper No. 9, filed 2/19/2002, is acknowledged. The traversal is on the ground(s) that: 1) the invention as claimed in the different groups can be readily evaluated in one search without putting an undue burden on the examiner because the claims are so interrelated, 2) Groups I and V are so interrelated that a search of the two groups individually will require a substantial duplication of work on the part of the Office, and 3) there would be an undue burden placed on applicant in requiring payment of a separate filing fee for examination of the nonelected claims as well as the added costs associated with prosecuting two applications and maintaining two patents. This is not found persuasive because of the following reasons.

Arguments directed towards undue search burden, duplication of effort and added costs are not persuasive regarding restriction of claims for National Stage Applications filed under 35 U.S.C. 371. The proper question is whether the inventions of the different groups have unity of invention (i.e. the inventions are linked to form a single inventive concept). The response filed in Paper No. 9 does not address the arguments put forth by the examiner in Paper No. 8 as to why the inventions of the different groups do not have unity of invention. For example, with regard to Groups I and V, the two groups do not share the same special technical feature. Group I is directed towards a process for characterization of a microbial gene wherein the gene is controllably expressed in a microbial cell in a mammal while Group V is directed towards controlled expression of a prokaryotic gene in a microbial cell in vitro. The special technical feature of Group I, controlled expression of a desired gene in a microbial cell that is located

within a multicellular animal, is not present in, or required for, the invention of Group V. Therefore, these inventions are not so linked as to form a single inventive concept under PCT Rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-77 are pending in this application. Claims 21-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Drawings

The drawings are objected to because Figure 5 erroneously indicates that the displayed nucleic acid sequence is SEQ ID NO: 39. According to the Brief Description of the Drawings and the sequence listing, the figure should be corrected to indicate that the sequence shown is SEQ ID NO: 37. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

Receipt is acknowledged of an information disclosure statement (IDS), filed 5/2/01 as Paper No. 5. The signed and initialed PTO Form 1449 has been mailed with this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 and 77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the preamble of the claim recites "A process to allow the characterization of a microbial gene or genes, here gene..." indicating that the process is directed at one or more genes, while referring many times to the process in the body of the claim as directed toward "said gene" (e.g. line 3). This inconsistency makes unclear the antecedent basis for "said gene" and "said genes" throughout the remainder of the claim and in subsequent dependent claims. This inconsistency also makes it unclear as to whether the recited process can be practiced with more than one gene that encodes a gene target. The preamble is also vague and indefinite in that the process outlined in the remainder of the claim appears to be one directed at actual characterization of a microbial gene rather than one that "allows" characterization of the gene. It would be remedial to delete the words "to allow" from the claim language. Finally, the words "here gene" do not appear to tie in with the rest of the claim at all, making it unclear as to what limitation is referred to by the words "here gene". It would be remedial to amend the claim language by deleting the words "here gene" as they do not appear to add anything to the claim.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "...where said gene target is important to a microbe's ability to infect or sustain an infection in a mammal..." are unclear. The phrase is unclear in that it implies that it is known prior to practicing the claimed method that the gene target is important in the infection process for a given microbe.

However, upon reading the specification and reading the remainder of the claim language, it appears that the claimed method is intended to determine whether target genes actually are important in the process of infection for a given microbe and host animal. It would be remedial to amend the claim language to clearly indicate whether or not one must know before practicing the claimed method that the target gene is important in infection of the host animal by the microbe.

Claim 1 is vague and indefinite in that it recites the limitation "...that controls the expression of the target gene or gene product..." (line 11), implying that the target gene and gene product can be different from one another. Earlier in the claim, in lines 3-4, it is specified that the gene target and gene product are the same and that the same microbial gene encodes them. It would be remedial to amend the claim language to clarify whether the gene target and gene product are the same, and if so, to remove any language that implies that they are different from one another.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd.

App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the phrase "...where said gene, which may be any gene which encodes a microbial protein, or more generally a microbial gene product..." (lines 15-16). This phrase comprises the broad recitation "...where said gene ...or more generally a microbial gene product..." along with the narrower statement "...which may be any gene which encodes a microbial gene...". The term microbial gene product encompasses both RNA and protein products.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "...where said mammal is a plurality of at least two or more mammals with said mammals are initially exposed to tetracycline and infected with said genetically altered microbe..." are unclear. First, the phrase is grammatically incorrect (e.g. "with said mammals are initially"). Secondly, it is unclear how a single mammal can also be a plurality of mammals. Finally, it is unclear whether the limitation "initially" is applied to just the step of exposing the animals to tetracycline or whether the term also encompasses the step of infecting the host animals. Do the steps of exposing the animals to tetracycline and infecting the animals with the genetically altered microbes necessarily occur at the same time? It would be remedial to amend the claim language to clearly indicate that the method is practiced with test and control mammals and also whether the steps of exposing the animals to tetracycline and infecting the animals are both part of an "initial" step, or not.

Claim 1 is also vague and indefinite in that the metes and bounds of the phrase "meaningful difference between the two groups of animals" are not clear. The term "meaningful difference" does not appear to be clearly defined in the specification and is inherently indefinite.

What constitutes a "meaningful difference" with regard to degree of infection, microbe levels, or physiological conditions of the animals is likely to differ from investigator to investigator. It would be remedial to amend the claim language to clearly indicate what are the metes and bounds of the term "meaningful difference" between the test and control animals.

Claims 2, 4, and 7 are vague and indefinite in that the metes and bounds of the phrase "...and where said TCE is comprised of a tetracycline-controllable transcription promoter polynucleotide sequence, operably linked to a polynucleotide sequence encoding a reporter gene..." are unclear. First, it is unclear whether the term "is comprised of" is open or closed language (e.g. "comprising" versus "consisting of"). The cited phrase is also unclear in that it implies that the TCE comprises a reporter coding sequence (and a target gene sequence for claims 4 and 7) when the specification apparently teaches that the minimal parts required for a TCE element are a promoter operatively linked to TetR binding sequences (e.g. page 13, lines 6-13). It would be remedial to amend the claim language to clearly indicate whether the TCE comprises elements in addition to the tetracycline-controllable transcription promoter polynucleotide sequence.

Claim 5 is vague and indefinite in that it implies that a gene is actually a protein (i.e. "said reporter gene is B-lactamase"). It would be remedial to amend the claim language to indicate the reporter gene "encodes" B-lactamase.

Claim 6 is vague and indefinite in that the metes and bounds of the phrase "...additional alterations comprising a tetracycline resistance (or protection) and repressor DNA cassette (TRRDC)..." are unclear. It is unclear whether the words in parenthesis, "or protection", specify an additional claim limitation or not, and if they do, what they are intended to specify. Upon

reading the specification, it appears the phrase is meant to specify a tetracycline resistance gene as well as a gene encoding a tetracycline-responsive repressor. Also, the term (TRRDC) implies that the two genes are together on the same cassette. The claim language, however, does not clearly indicate that the two genes, encoding a resistance protein and a repressor protein, are necessarily operatively linked on the same piece of DNA. It would be remedial to amend the claim language to more clearly indicate what coding sequences are being specified as part of the TRRDC and how they are intended to be linked in such a cassette.

Claim 8 is vague and indefinite in that the metes and bounds of the phrase "...and where a promoter is operatively linked to the TCE..." are unclear. The phrase is unclear in that the specification teaches that the TCE necessarily comprises a functional promoter operatively linked to binding sites (tetO) for the tetracycline repressor (tetR). Does the cited phrase specify that a second, different promoter is also operatively linked to the TCE? It would be remedial to amend the claim language to clearly indicate whether the limitation of "a promoter operatively linked to the TCE" specifies a second promoter operatively linked to the TCE and, if so, how it is linked (e.g. is it also responsive to the tet repressor?).

Claims 9 and 10 are vague and indefinite in that the metes and bounds of the term "mathematically significant difference" are unclear. It is unclear exactly what constitutes a "mathematically significant" difference in survival rates, microbe levels or infection levels in the host animals. The term is not clearly defined in the specification and is likely to vary from investigator to investigator. It would be remedial to amend the claim language to clearly indicate what constitutes a "mathematically significant" difference in survival rates, microbe levels or infection levels for the host animals.

Claim 11 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said significant difference" in claim 11, or in claim 10, upon which claim 11 is dependent.

Claim 12 is vague and indefinite in that the metes and bounds of the phrase "is comprised of" are unclear. Is this open or closed claim language (e.g. "comprising" versus "consisting of")? Given the nature of the TRRDC, as described in the claims and specification, it would be remedial to amend the claim language to clearly indicate the TRRDC comprises the tetM coding sequence.

Claim 13 is vague and indefinite in that the metes and bounds of the words "derived from" are unclear. The words imply additional steps that may or may not change the character of the recited object (i.e. the tet repressor gene) after obtaining it from the recited source (i.e. the Tn10 transposon). It is unclear the nature and number of steps required to obtain such a "derivative". It would be remedial to amend the claim language by replacing the words "derived from" with the words "obtained from".

Claim 14 is vague and indefinite in that the metes and bounds of the phrase "...wherein said Tn10 transposon is selected from the sequence of SEQ. ID. NO. 35 and 36..." are unclear. First, SEQ ID NOS: 35 and 36 are slightly different sequences and it is confusing to refer to them as a single sequence when they are not. Also, the sequences recited in SEQ ID NOS: 35 and 36 do not comprise a full transposon. They only comprise sequences associated with the coding sequence for tetM. It appears that claim 14 may have been meant to be dependent upon claim 12 and specify that the sequences from the tetM gene comprise sequences recited in SEQ ID NOS: 35 or 36. A proper way to refer to the sequence identifiers would be "SEQ ID NO: 35

or SEQ ID NO: 36" or "SEQ ID NO: 35 and SEQ ID NO: 36", depending on the kind of alternative language used in the amended claim.

Claim 15 is vague and indefinite in that there is no clear and positive prior antecedent basis for the words "said mammals" in claim 15, or in claim 1, upon which claim 15 is dependent.

Claim 16 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said recombinant bacterium" in claim 16, or in claim 1, upon which claim 16 is dependent.

Claim 17 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said Staphylococcus species" in claim 17, or in claim 1, upon which claim 16 is dependent.

Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: any sort of functional linkage between the endogenous prokaryotic gene and the step of cultivating the prokaryotic cell in a mammalian host in the presence of a controlled amount of tetracycline.

Claim 77 is vague and indefinite in that the metes and bounds of the words "endogenous prokaryotic gene" are unclear. The words are unclear in that, in light of the specification, the term "endogenous" gene (i.e. the regulatory and coding sequences of a prokaryotic gene) may encompass genes that have been modified to comprise a heterologous element (e.g. the TCE) so that it is responsive to tetracycline. Alternatively, the term "endogenous" gene could be intended to encompass only those genes that comprise native regulatory and coding sequences (e.g. in

embodiments of the methods of the invention where anti-sense polynucleotides or ribozymes are used to control expression of a target gene). It would be remedial to amend the claim language to clearly indicate what types of genes are encompassed by the words "endogenous prokaryotic genes".

Claim 77 is vague and indefinite in that the metes and bounds of the phrase "controlled amount of tetracycline or tetracycline analog..." are unclear. The term "controlled amount" does not appear to be clearly defined in the specification. Does the term "controlled amount" refer to the means in which the tetracycline is delivered to the mammal? Or does it refer to a specific amount of the drug that is given to the animal? It would be remedial to amend the claim language to more clearly indicate the requirements for an amount of tetracycline administered to a host mammal to be considered as a "controlled amount".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The claimed invention is drawn towards a process to allow characterization of a microbial gene with regard to its importance in the ability of the microbe to initiate or sustain infection. The method utilizes a tetracycline-responsive promoter (the TCE) to drive expression of a polynucleotide such that the amount of a target gene product encoded by one of the microbial genes is regulated by the presence or absence of tetracycline. A genetically altered microorganism comprising the TCE is used to infect at least two or more mammals at the same time that the animals are exposed to tetracycline such that the function of the targeted microbial gene is regulated. Tetracycline is then removed from a portion of the population of mammals. The degree of infection, number of microbes (i.e. microbe levels) and physiological condition of the mammals is determined for both sets of infected animals (i.e. +/- tetracycline) and the results compared to one another. A "meaningful difference" between the two groups of infected animals indicates the identification of a gene that is important to a microbe's ability to infect, or sustain infection of, a mammal. The tet-responsive promoter can be a prokaryotic promoter. The "meaningful difference" can be a "mathematically significant difference" (although neither term is clearly defined in the specification and claims 9-11 thus read on any quantifiable difference in pathogenicity between the two groups of infected animals). The host mammals can be mice. The microbes can be recombinant bacteria, a virus or yeast. Specifically, the microbe can be Staphylococcus aureus. The Bostian et al reference of the following rejection teaches each of the above limitations, including the removal of the inducer (i.e. tetracycline) to regulate the target gene function, but does not explicitly teach the use of control animals. The Setterstrom

et al reference teaches the use of control animals to provide a clear standard for microbial infection for comparison to test animals where microbial infection has been altered due to interference with at least one gene function (e.g. through the use of antibiotics).

Claims 1, 3, 9-11 and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bostian et al (WO 96/40979, 19 December 1996; see the entire document) in view of Setterstrom et al (U.S. Patent No. 6,309,669 B1; see the entire patent).

Bostian et al teach methods for evaluating microbial genes as targets for compounds which inhibit the pathogenesis of a microbe, and for evaluating the expected therapeutic effect of compounds which inhibit a reaction of a microbial cell which is related to the expression of a specific gene (i.e. the "gene target" of the instant invention). The methods utilize recombinant microbes which contain DNA constructs or alterations (i.e. the "switches" of the Bostian et al application) that allow the level of activity of the products of coding regions associated with those constructs or alterations to be controlled by the presence or absence of a specific small molecule or "switching compound" at any of several points in the infection process (e.g. Abstract; page 17, lines 3-21; page 4, lines 4-19). The expression of the coding regions associated with the DNA constructs or alterations is designed to affect the activity of the specific gene target in the microbe while the microbe is in the process of infecting a host organism. The methods comprise infecting an animal or plant model host with a genetically altered microbe where the genetic alteration causes a change in the level of activity of a product of the coding sequence of a putative pathogenesis gene or essential gene in the microbe in response to an environmental change (e.g. exposure to a switching compound) and determining whether the

state of infection or condition of the host is changed as a result of altering the level of activity of the target gene or gene product. In some cases the level of activity of the target gene is affected by the administration of the switching compound to the host animal. In other instances, the level of activity of the target gene is regulated by removing or decreasing the concentration of the switching compound (e.g. page 26, lines 14-31; examiner's emphasis added).

The DNA constructs or "alterations" used in the invention taught by Bostian et al comprise repressor/operator pairs used as regulatory "switches" to control expression of a coding sequence that affects the functional activity of the target gene (e.g. Figure 3; page 41 lines 3-29). A preferred switching compound of the system is tetracycline, used in conjunction with a promoter operatively linked to operator sequences (i.e. tetO) that specifically bind to the tetracycline repressor (tetR) (e.g. page 17, lines 3-21; page 41, lines 3-29; page 54, lines 15-17). A switching compound of the invention can cause a decrease or an increase in the level of activity of a coding sequence, depending upon the type of DNA construct or alteration used (e.g. sense or antisense expressed and the type of repressor/operator construct) (e.g. pages 56-57). The small molecule-responsive "switches" of the invention can be directly linked to an endogenous target gene of interest (e.g. by integration of a switch construct into a bacterial chromosome such that a chromosomal gene is now responsive to the small molecule "switcher") or indirectly linked by a second repressor/operator element (e.g. Figure 3; page 7, lines 1-17; page 29, lines 12-16).

In the methods taught by Bostian et al, the putative pathogenesis gene or essential gene is a valid target if the state of the infection or the physiological condition of the host is altered in response to the change in level of activity of the target gene (e.g. page 5, lines 16-35). Criteria

for evaluation in the host include the ability of the microbe to replicate (the test gene expression can be "on" or "off"), the ability to produce specific exoproducts involved in virulence of the organism, and the ability to cause symptoms of disease in the animals (e.g. page 49, lines 14-19). Acceptable mammalian animal models for use in the system include mice, rats, rabbits, dogs, cats and swine (e.g. page 13, lines 24-27; Examples 5-10). Microbes that can be used in the methods described by Bostian et al include bacteria, protozoa, fungi, yeast and viruses. Staphylococcus aureus is a bacterial microbe described as useful in the methods of the invention (page 14, lines 9-14). Bostian et al teach several different specific animal model systems for studying the effects of altering gene expression on infection of a host animal by a microbe (e.g. the Mouse Soft Tissue Model, the rabbit Osteomyelitis model, etc.; see Examples 5-10).

Bostian et al do not explicitly teach the use of control animals in their methods where the target gene function in the infecting microbe has not been inhibited (i.e. a "normal" infection control).

Setterstrom et al teach the use of novel burst-free, sustained release biocompatible and biodegradable microcapsules that can be programmed to release their active core (e.g. an antibiotic) for variable durations ranging from 1-100 days in an aqueous physiological environment (e.g. the Abstract). Setterstrom et al teach a set of examples wherein the rabbit osteomyelitis animal model system is used to demonstrate the efficacy of their invention (e.g. Section VII, Examples 1-7 beginning at column 40 and continuing through column 45, line 60). In these examples, Staphylococcus aureus preparations were used to infect the tibial metaphysis of laboratory rabbits (e.g. Example 1). Antibiotic therapy using the compositions of the Setterstrom et al invention was initiated immediately or delayed for 7-days. For each infected

animal the infected tibia was harvested and used to determine the extent of infection (e.g. Example 6). Whether treatment was initiated immediately or postponed for seven days post-infection, the experiments were conducted with control animals that were infected with S. aureus and received no antibiotic treatment (e.g. Examples 3 & 4).

It would have been obvious to one of ordinary skill in the art at the time of applicants' invention to modify the methods taught by Bostian et al for the characterization of potential antimicrobial gene targets (e.g. removal tetracycline to control target gene function in a microbe during infection) to include the use of control animals where the activity of the gene target is not inhibited (e.g. where the tetracycline concentration is maintained) because Bostian et al teach it is within the skill of the art to utilize a tetracycline-responsive system to control the level of activity of a gene target in a microbe during the process of infection and because Setterstrom et al teach it is within the skill of the art to utilize a control animal to provide a clear contrast between treatment or nontreatment of infection. One would have been motivated to do so in order to receive the expected benefit, as exemplified by Setterstrom et al, of being able to compare the level of infection in an animal in which no target gene has been inactivated (e.g. the untreated animals of Setterstrom et al) with an animal in which at least one gene function has been altered (e.g. the animals treated with antibiotics as taught by Setterstrom et al). Absent any evidence to the contrary, there would have been a reasonable expectation of success in using a control animal, as taught by Setterstrom et al, in the methods taught by Bostian et al to provide a clear background for comparison of the effects of target gene inactivation.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 746-5114 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

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May 6, 2002